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NEWSLETTER OF THE NCI DIVISION OF CANCER PREVENTION

IN THIS ISSUE

Nanotechnology Not So Exotic

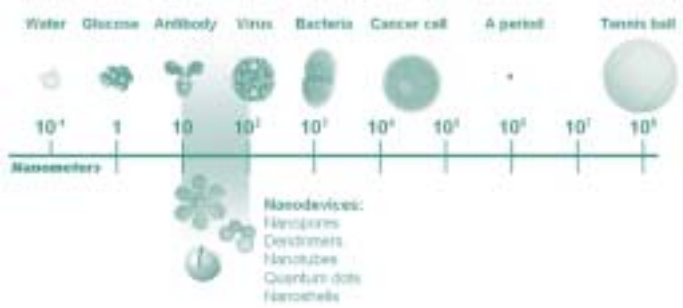
PAUL WAGNER

Nanotechnology has been extensively discussed in both the popular press and scientific journals, yet a surprisingly large number of us have no clear understanding of what nanotechnology is or, worse, have a complete misunderstanding. This confusion results in part from attempts by some scientists and journalists to mystify and hype this technology; they speculate that nanotechnology will restore the world's ecology, prolong life, and provide for unlimited wealth. Adding to the confusion are alarmist articles, especially in the European press, and Michael Crichton's highly entertaining novel *Prey*, which depicts self-replicating nanorobots that feed on their human creators. One person who has reacted, or some would say overreacted, to these concerns is Prince Charles, who has requested that the United Kingdom's Royal Society hold an inquest into the perils of nanotechnology. Thus, the casual reader may come away wondering whether nanotechnology is the savior of mankind or a demon that, once let out of the bottle, will lead inexorably to our demise.

Most nanotechnologists believe that nanorobots will not be developed any time soon, and their current research concerns nanosized particles of organic and inorganic matter. Nanotechnology, unlike most fields of science, is not concerned with a specific area of research but rather with size; it is the creation of materials, devices, and systems through the manipulation of matter on the nanometer scale. A nanometer is one billionth of a meter or, as commonly described, 1/10,000 the width of a human hair. Thus, the field of nanotechnology involves scientists from many disciplines, including material scientists, chemists, engineers, and biologists. Working with materials with one dimension less than 100 nanometers is also considered nanoscience, and coating microchips with a nanometer-thick layer is nanotechnology.

One reason for the interest in nanoscience is that physical, chemical, and biological properties of materials differ fundamentally at the nanoscale, resulting in unusual but exploitable behaviors. The two basic approaches for creating nanomaterials are termed "top-down" and "bottom-up." The top-down approach involves etching or molding materials into smaller and smaller components and is used in electronics and computers. The bottom-up approach involves assembling structures atom-by-atom or molecule-by-molecule and is relevant to medical devices. Nanotechnology is already in use in a few commercially available products, including sunscreens, tennis racquets, fishing rods, stain-resistant pants, and Jumbotron lamps, which are used to light many athletic stadiums.

The National Institutes of Health defines nanomedicine as medical treatment at the level of single molecules or molecular assemblies at the scale of about 100 nanometers or less. The usefulness of nanotechnology for medicine stems from the fact that nanoscale devices are of the same size as biological entities. They are smaller than human cells (a white blood cell is about 10,000 nanometers in diameter) and similar in size to enzymes and receptors; hemoglobin is approximately 5 nanometers in diameter and the cell membrane is approximately 6 nanometers thick.



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You've probably noticed...

SUSAN N. PERKINS, EDITOR-IN-CHIEF

Our new look! This is our tenth issue, and the new color scheme is in part a celebration of that milestone. Although what I have fondly thought of as "**PreventionPOST** Purple" has made the newsletter instantly identifiable, the sameness from one issue to the next has sometimes made for confusion about when and whether a new edition has appeared. Thus, from here on we intend to rotate colors, thereby making each new issue immediately recognizable when it hits the displays and news boxes. Also starting with this issue, we are sending out an email announcement about each edition to bring its publication to the attention of our readership.

A much less superficial change with this edition is the inauguration of a new feature in the part of the newsletter devoted to the Cancer Prevention Fellowship Program. Called "Beyond the Fellowship Program," this new section will recognize fellows who have recently completed the fellowship program and will list the institutions and organizations where they will pursue the next step in their careers.

Many thanks to those of you who took the time to respond to the recent survey on the newsletter in spite of the avalanche of such requests that arrive with each day's email. We greatly appreciated the compliments we received and will take into careful consideration both the helpful suggestions and the thoughtful criticisms when we begin planning the next issue. One request that we cannot accommodate is for a more frequent publication schedule: unlike some other newsletters you now see in circulation, ours is conceived, written, crafted, and designed by an all-volunteer team who need to keep up with their day jobs.

One fact brought to light by the survey was that many readers are not aware that an electronic version of the newsletter is available. The **PreventionPOST** is posted on line soon after the print edition appears in your mailbox. Furthermore, all back issues are accessible at http://www3.cancer.gov/prevention/about.html#pp. You can also find the newsletter by going to the DCP home web page and clicking on "About the Division of Cancer Prevention (DCP)."

Finally, the goal of the DCP Newsletter Project Team is to make your newsletter as useful and relevant to the Division as possible. Please feel free to send any and all suggestions, comments, and criticisms to pp_editor@ncifcrf.gov. And, as always, I invite anyone who would like to see his or her ideas for the newsletter become reality to join us. Thank you again for your interest in the newsletter. ■

The Contract as a Funding Mechanism

GRANT IZMIRLIAN AND EVA SZABO

The National Cancer Act of 1971 directs the National Cancer Institute (NCI) to "plan and develop an expanded, intensified, and coordinated cancer research program encompassing the programs of the NCI, related programs of other research institutes, and other Federal and non-Federal programs." To carry out this mission, the NCI utilizes a number of funding mechanisms, including contracts, grants, and cooperative agreements, to conduct and support cancer-related activities on the nature, prevention, detection, diagnosis, and treatment of cancer.

As a general rule, the NCI utilizes contracts when the principal purpose of a transaction is to acquire goods or services for the direct benefit of the Federal Government, and uses grants or cooperative agreements when the principal purpose is to assist or support an organization that is performing a public purpose. Research contracts are of two major types: research/development and research/development support. The contract funding mechanism is used by the funding agency to obtain specific goods or services under specific conditions. The main difference between contracts and grants/cooperative agreements is that the former spell out what is to be done and how it is to be accomplished. Furthermore, in addition to affording the Government more control in the design of the research objectives, the contract funding mechanism gives the Government control over the pace of completion and insurances against default.

To better understand these differences, consider the goals and results obtained from successful research programs funded by the different mechanisms. Investigator-initiated research is driven by relevant research questions and the interests/capabilities of the individual investigator. When gaps in research are identified, the investigator-initiated pool of applications may not necessarily address the gaps and has no obligation to do so. The NCI will frequently turn to cooperative agreements to stimulate research in specific areas, but, again, the responses from the research community will not necessarily answer very specific questions that exist. When specific questions need to be answered, the contract mechanism offers an opportunity to "fill in the gaps." As a case in point, this article highlights the funding of the newly established Cancer Prevention Consortia, established in order to conduct phase I and phase II trials of investigative cancer preventive agents.

The contract mechanism was chosen as the funding mechanism for the Prevention Consortia for several reasons. First, it

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Bernardino Ramazzini: Father of Preventive Medicine for the Workplace

KATHLEEN FOSTER

Bernardino Ramazzini entered the world in 1633, during a time of widespread chaos. Most of Europe was in the grip of the Thirty Years War, a political and religious struggle that decimated a great deal of the population. The creative thinking that had flourished throughout the era of the Renaissance had laid the foundations for modern science. However, in Italy the 17th century brought with it a repressive political climate that discouraged any innovative opinions. In Rome, the teachings of Copernicus and Galileo Galilei had been banned by the Council of the Inquisition. Despite this oppressive mentality, the fears that had dominated the medieval consciousness were easing. As a result of a better understanding of public sanitation and of disease control through quarantine, the constant sense of foreboding that had centered on the Bubonic Plague was now vanquished.

Bernardino Ramazzini

Born in a small northern Italian town, Ramazzini was a son of middle-class parents, yet he benefited from an early Jesuit education. He graduated from the University of Parma with a degree in Philosophy and Medicine and started a long and productive career as a doctor and teacher. Continuing his education in Rome, the young scholar developed an interest in the variety of craftsmen plying their various trades in the bustling city. This academic interest led to a concern for the welfare of workers that ultimately shaped his career. Initially, Ramazzini's intellectual curiosity was piqued by the health conditions of the workforce in Italy's tanneries and foundries. Although others before him had observed a relationship between workplace hazards and poor health, Dr. Ramazzini was the first to systematically describe the symptoms and diseases and to correlate them with the type of work performed.

In 1671, after practicing medicine for many years, the celebrated scientist accepted an appointment as Chair of Theory of Medicine at the renowned University at Modena. Despite his new appointment, Ramazzini was always one to challenge the conventional thinking. It was common practice for his contemporaries to prescribe the same wonder drug of the time for all types of fever, that being cinchona bark, from which the alkaloid quinine is derived. However, Ramazzini had contracted malaria himself as a youth, and he disputed this overuse and recommended that the drug be reserved exclusively for the treatment of malarial attacks.

Despite Professor Ramazzini's other regular duties he continued to pursue his fascination with work-related health hazards and became an expert on the subject of occupation-associated illness, visiting work sites and interviewing the various craftsmen about their symptoms. This activity was met with hostility on the part of his peers, who considered it demeaning to interact with common laborers. Despite their opposition, he persevered and pursued his vision of preventing illness by obtaining a better understanding of occupational causes. It was during the 1690s that Ramazzini performed the first real epidemiological works that were to ensure his place in the annals of preventive medicine.

One scenario that first caught the attention of Ramazzini was the behavior of a sewage worker who labored with great rapidity at his task. When asked why the haste, the worker replied that those who lingered too long at the job frequently became blind. The inquisitive physician went on to postulate that prolonged exposure to ammonia vapors could ultimately cause eye damage. Another of his observations established the relationship between paint and the metallic poisoning of painters. He went on to pursue his research and to document conditions related to fifty-two different occupations, such as apothecaries, makers of lute strings, and tobacco workers. Due to his scrupulous observations he was able to record the fact that noxious vapors and very fine particles, such as mineral powders inhaled by miners and stonecutters, can be absorbed through the lungs. As evidence of his truly advanced worldview, Ramazzini also concerned himself with the conditions of female workers by recommending standards of hygiene for midwives and precautions against syphilis.

One of Ramazzini's major contributions was expanding the Hippocratic method of questioning cause, duration, and symptoms of each illness to include environmental influences. His systematic approach encompassed the details of each job, clinical presentation, a review of the literature, and recommendations for treatment and workplace guidelines. His approach was innovative in that it anticipated the epidemiological principles of modern science by placing the illness in the context of the workplace and by using logical deductions to form a diagnosis and to develop recommendations for change.

Another of his accomplishments was anticipating the modern-day science of ergonomics by understanding that repetitive motion and poor body mechanics can be a source of disability. As stated in his famed treatise on occupational diseases, *De Morbis Artificium Diatribe* (*Diseases of Workers)*, "Nature delights and is restored by alternating and varied actions."

Not content to deal only in academics, this champion of preventive medicine took his observations to the workers themselves. His goal was to inform them on how to prevent their occupational injuries. Ramazzini counseled the laborers to be mindful of the risks inherent in the performance of their jobs and to adopt personal protective measures.

After the publication of his seminal work in 1700, the versatile scholar, clinician, and author was invited to the University of Padua, where he held the chair of Practical Medicine and taught until his death in1714. The foresight and original research of this prevention pioneer has earned him the title of "Father of Occupational Medicine." ■

Nanotechnology Not So Exotic continued from page 1

Nanodevices can interact with cell surface receptors, and those smaller than 50 nanometers can easily enter cells and interact with cellular DNA and proteins and, thereby, alter the cell's behavior or even destroy it.

What are medical nanodevices if they are not tiny little robots or submarines that circulate in the body repairing damaged cells and tissues or destroying abnormal cells and pathogens? Some medical nanodevices are based on biological structures such as viruses and liposomes. Cross-linked liposomes and engineered viral particles containing drugs and/or imaging probes can be targeted to specific cells or tissues by attaching antibodies or other homing molecules to their surfaces. Nanoshells are another type of device that has medical applications. Nanoshells are hollow spheres made of silica and are sometimes coated with gold. They can be filled with drug-containing polymers, and antibodies can be attached to their surfaces to target them to specific types of cells. Laser light directed onto these nanoshells from outside of the body can heat the shells, causing them to release a controlled amount of the drug. Heating nanoshells bound to tumor cells can also cause them to superheat, destroying tumor cells and leaving healthy cells unaffected. Other medical nanodevices are based on buckyballs (60-carbon atoms arranged in the shape of a soccer ball), chemically functionalized dendrimers (protein-sized spherical polymers made from acrylic acid and a diamine), nanotubes (carbon rods about half the diameter of a molecule of DNA), and quantum dots (tiny crystals that act as molecular light sources). An attribute common to many of these nanodevices is the ability to target large amounts of contrast agents, therapeutics, or other biologically active agents to specific cell types. It is this targeting and the resulting specificity that excites many medical nanotechnologists.

Dr. Anna Barker, NCI Deputy Director for Advanced Technologies and Strategic Partnerships, has written, "Nanotechnology... has the potential to yield new devices that could transform cancer prevention, early detection, imaging, and smart therapeutics." Nanotechnology can contribute to the development of carriers that more effectively deliver cancer prevention agents and anticancer vaccines. Multifunctional nanocarriers, intermixed with our daily diet, may increase in the efficacy of the oral administration of cancer-preventing *nutraceuticals*. Nanotechnology is already having an impact on cancer imaging. The cores of nanoparticles can be made from a variety of materials that can be used as contrast agents for X-ray or CT imaging, Magnetic Resonance Imaging, PET, ultrasound, near-infrared surface scans, thermography, and nuclear imaging. A few antibodies attached to the surface of these nanoparticles can target tens of thousands of contrast agents to a single cell. Nanotechnology will be used to develop devices to eradicate cancer cells without harming healthy neighboring cells. These therapeutic agents will target specific cells and deliver toxins or drugs in a controlled, time-release manner. An ambitious goal of nanotechnology is to make a single nanoparticle that can detect cancer, deliver therapy, and monitor the efficacy of treatment.

The current projected uses of nanotechnology in medicine may not be as exotic as self-replicating nanorobots, but they do have the potential to revolutionize how we detect and treat cancers. So, are the fears of nanorobots and ecological disaster completely unfounded? Maybe not. Some scientists and futurists still predict the development of self-replicating, self-propelled nanorobots, parts of which will be based on biological organisms. Also, as reported by Rick Weiss in *The Washington Post* in May 2004, "Of particular interest to regulators and toxicologists is the emergence of evidence that some substances that that are normally biologically inert can cause worrisome reactions in the body when present as nanoparticles. Similarly, some substances that are normally safe in the environment seem to have the potential to be ecologically disruptive when dispersed as nano-size particles." Thus, as with any new technology, it is important that we be aware of nanotechnology's promises and limitations and pay attention to any potential unwanted side effects. ■

PreventionPOST

The DCP Newsletter welcomes returning member Susan Winer!

DCP Newsletter Project Team

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Back issues of the *PreventionPOST* may be seen online at
http://www3.cancer.gov/prevention/about.html#pp

Encouraging the Next Generation of Prevention Scientists

ANN O'MARA

The Cancer Prevention Fellowship program remains an important mechanism for the Division to mentor and recruit scientists into the field of cancer prevention. However, did you know that we can start the mentoring process even earlier, such as at the pre-baccalaureate level? This summer the Division supported two undergraduate students, one in the Office of Preventive Oncology (OPO) and the other in the Nutritional Sciences Research Group (NSRG).

While the Cancer Research Training Award (CRTA) is the "umbrella" appointment mechanism for the Division's Cancer Prevention Fellowship Program, this mechanism is not limited to individuals with doctoral degrees, nor does the candidate have to commit to a full-time experience. Our two undergraduate students, Karen Mayer in OPO and Behzad Varamini in NSRG, were here as CRTAs, gaining knowledge and experience during their summer vacation from school. The routes they used to get to our Division are interesting and should provide us with some ideas on how to attract more budding scientists to the field of cancer prevention.

Behzad Varamini and Karen Mayer

Karen is a sophomore at the University of Maryland College Park, majoring in neurobiology and physiology. Her career goal is to attend medical school and eventually specialize in the field of pediatrics, an excellent area in which to study and ultimately practice the principles of disease prevention. In her search for a summer job, she discovered the CRTA program on the web and contacted Dr. Shine Chang in OPO. Her responsibilities included creating flow charts to help the incoming fellows understand how to arrange travel to local, domestic, and international conferences, as well helping the OPO staff prepare for the new class of Prevention Fellows.

This was Behzad's second year in the NSRG. He is a recent graduate of Elizabethtown College, Elizabethtown, PA, with a Bachelor of Science degree in biotechnology. While his career goals are not totally firmed up yet, he is interested in disease prevention. During his junior year, he attended a seminar on cancer prevention at Hershey Medical Center. One particular presenter, our own John Milner, caught his attention and he contacted him. Through a series of email correspondences and eventually an application, Behzad was hired last summer as a CRTA student and continued in this role this summer. He has attended several large nutrition and cancer-related conferences and this summer worked on assembling a review article about aberrant crypt foci and bioactive food components with Dr. Milner. He will begin doctoral studies in nutritional sciences at Cornell University this fall and hopes to continue working at the National Institutes of Health in one capacity or another in the future.

More information on the CRTA program can be found at http://camp.nci.nih.gov/admin/crta/. ■

Nutrition and Cancer Prevention Practicum

BY CINDY DAVIS AND ELAINE TRUJILLO

The first-ever Nutrition and Cancer Prevention Practicum was held March 15 through March 19. The Nutritional Science Research Group in the Division of Cancer Prevention, National Cancer Institute (NCI)/National Institutes of Health (NIH), and the Department of Nutrition at the Clinical Center, NIH, joined forces to co-sponsor this event. Sixteen outstanding nutrition students and dietetic interns from around the country attended this training.

This one-week session provided specialized instruction in diverse topics, such as the latest cancer trends from the NCI's Surveillance Research Group, clinical intervention studies, bioactive food components (including selenium, indole-3-carbinol, tea polyphenols, garlic, and antioxidants), obesity and energy balance in relation to cancer, new technologies in cancer research, bioethics, palliative care, and health claims and messages. The participants also learned about the role of the research dietitian in grant involvement and clinical intervention studies, including how clinical intervention studies are coordinated at a national level. The faculty for the lectures consisted of experts from the NIH and from academic institutions. In addition there was a tour of the metabolic kitchen at the Beltsville Human Nutrition Research Center, which is part of USDA. There was also a special "Research Day" with 50 local dietetic interns. The research day included hands-on workshops on body composition and dietary supplements and a tour of the clinical center.

Students sharpened their research skills by spending part of their time each day investigating a select nutrient and how it relates to cancer prevention. Finally, on the last day of the practicum, participants summarized their findings and presented their results. ■

Practicum Participants Top row (left to right): Steve Carrington, Young Kim, MariAnn Wheeler, Nylia Ramos Kreiner, Elaine Trujillo. Middle row: Anne Newton, Jennifer Stokols, Jenny Hatch, Ana Blanco, Kristen Schulthess, Bridgete Smith, Jennifer Hicks, Bonnie Peck, Adriene Knight, John Milner, Rachael Drabot, Harold Seifreid, Emily Kehoe, Jackie Whitted. Bottom row: Olivia Ho, Sarah Golden, Alana Alexander.

On the Brink of Pre-emption: Breast and Gynecologic Cancer Research Group

DORIS BROWNE

An estimated 217,440 new cases of invasive breast cancer (BC) will be diagnosed in the United States in 2004 and an estimated 40,110 women will die from the disease. The estimated numbers for reproductive cancers are 25,580 new ovarian cases, 16,090 deaths; 40,320 new endometrial cases, 7,090 deaths; and 10,520 new cervical cases, 3,900 deaths. Despite improvements in screening and early detection rates, treatment advances, and adoption of healthier lifestyles, breast cancer remains the most common non-skin cancer among women in the U.S. and the second leading cause of cancer death. Cervical cancer is a preventable and curable cancer if detected early, and although the incidence and mortality rates have declined by about 50% over the past three decades, it remains a very serious health threat.

Back row (left to right): Doris Browne, Medical Officer, Kathleen Foster, Nurse Specialist; Karen Johnson, Chief, BGRCG, Terri Cornelison, Medical Officer. Front row: Alfred Brown, Program Assistant; Diane Solomon, Medical Officer.

The mission of the Breast and Gynecologic Cancer Research Group (BGCRG) is to design, develop, implement, and monitor breast and gynecologic cancer research efforts. The focus is chemoprevention and nutrition, utilizing various prevention strategies that include pharmacologic, biologic, genetic, and proteomic interventions. Other research areas, such as cancer screening and early detection, vaccines, and immunologic interventions, are also priority areas.

BGCRG efforts are manifested through clinical research trials, screening, testing and validating new technologies that assist in identifying and modifying premalignant lesions. Team members monitor clinical trials designed to foster the development of new agents through modulation of surrogate endpoint biomarkers or cancer incidence reduction.

A team approach is taken towards managing our cancer research portfolios, which are designed to stimulate research leading to the development of preventive agents for breast and gynecologic cancers through various mechanisms. Some agents that serve as potential surrogate endpoints include those that work through a reduction in proliferation, protease inhibition, methylation inhibition, etc., as well as risk reduction.

While Tamoxifen is a proven effective prevention agent for estrogen receptor (ER)-positive BC, a similar agent is needed for prevention of ER-negative BC. The ER Negative Project Team chaired by BGCRG leadership is primarily focused on better identifying the natural history of ER-negative breast cancer; enumerating risk factors associated with ER-negative BC; reviewing mechanisms of action that are common to both ER-negative and ER-positive BC; identifying risk factors that are hormonally and non-hormonally related in ER-negative BC; developing new biological endpoints; and accelerating prevention agent development.

The ASCUS/LSIL Triage Study (ALTS), which involved over 5,000 women from four geographically diverse U.S. clinical centers, is the main focus of one of the BGCRG team members who serves as the Project Officer. This trial compared three different management strategies for women with equivocal or low grade cytology (Pap test) results. Although the trial ended in 2001, coordination of work continues on ALTS analyses and publications with the ALTS Co-Project Officer from DCEG. Over 20 manuscripts have been published, with over a dozen more in progress. Data from ALTS provided the basis for the development of evidence-based clinical consensus guidelines for managing women with abnormal cervical cytology.

Work continued over a span of 15 years to facilitate development of uniform laboratory terminology to report cervical cytology results, known as the Bethesda System. This terminology is used by over 90% of laboratories in the U.S. and also has been adopted by many international laboratories. The standard nomenclature allows comparisons of results across studies that would not be possible otherwise. The recently published second edition of the Bethesda Atlas sold over 7,000 copies in 3 months.

Team members review applications for clinical trials with emphasis on breast and gynecologic cancer prevention, help principal investigators develop protocols, manage awarded grants and contracts, and promote collaboration among researchers in areas leading to the development of surrogate endpoint biomarkers for new prevention agents. Gynecologic activities of the Team center on actively encouraging young investigators to focus their research on gynecologic cancer prevention, to submit grant applications, and to submit Letters of Intent (LOI) for contracts. One ongoing project of high interest is the conjugated estrogen and medroxyprogesterone acetate study in women at increased risk for developing endometrial cancer, which will answer questions on modulating biomarkers predictive of prevention.

Currently critical and exciting studies for breast cancer include COX-2 inhibitors; Tamoxifen compared to placebo; COX-2 and aromatase inhibitor comparison; and studies evaluating soy isoflavones and non-steroidal anti-inflammatory drugs. Outcomes are focused on proliferation changes, sampling techniques such ductal lavage, fine needle aspiration, and imaging.

To further promote gynecologic and breast malignancies prevention, the Team serves as project officers for NCI-funded grants by providing guidance for investigators regarding scientific merit and study design and monitoring research progress throughout the funding cycle. Team members are also involved in institute-wide activities that, although not solely related to cancer prevention certainly have impact on women's

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On the Brink of Pre-emption continued from page 6

cancer research and prevention science in general. These activities include serving as consultants and reviewers to Cancer Prevention and Control Concept Review; Protocol Review Committees; Community Clinical Oncology (CCOP) Program Research Bases; NCI Gynecologic Cancers Progress Review Group (PRG); NCI Breast Cancer PRG; Gynecologic Cancers PRG Implementation Working Group; HPV-Cervix Working Group; and Office of Education and Special Initiatives Risk Working Group. Additionally, a Team member sits on the Cancer Prevention and Control Committee and the Vaccine Sub-Committee of the Gynecologic Oncology Group.

In addition to four physicians the Team has a Nurse Specialist, whose responsibilities include serving as co-project officer for selected Consortia (the new funding mechanism concept that addresses multi-institutional cancer prevention research), as well as liaison to coordinators for ongoing chemoprevention studies. One aspect of this task involves co-chairing the annual Site Coordinators Opportunity for Research Excellence (SCORE) training workshop. Another aspect includes managing the Team's portfolio as the grants specialist. Other activities include participation in the Division's Project Teams such as the **PreventionPost** Newsletter, the Web Team, and the Committee to Optimize Recruitment, Retention and Adherence (CORRA). The Nurse Specialist also contributes to the CCOP review process.

Not only does the Team consist of physicians and a nurse, but it also has an Administrative Assistant (AA). The AA maintains the office decorum and keeps this very diverse, busy staff *on pointe* for the numerous activities, travel plans, policies, and procedures. Our support staff is essential to the Team's successful outcome.

Additionally, our work serves as a stimulus for minority investigators to become involved in prevention research, including greater participation in clinical trials and in designing and conducting preventive research studies. It is the interest of the Team to focus research efforts on critical questions addressing health disparities in breast and gynecologic cancer prevention and integrating minority investigators in information exchange forum and research opportunities. Specifically, ER-negative BC occurs in a higher percentage of African American women, and the Hispanic population has the highest numbers of cervical cancer cases.

The future of cervical cancer prevention will likely involve vaccines against human papillomavirus (HPV). An area of primary focus in gynecologic cancers has been to facilitate development of both treatment and prevention HPV vaccines into clinical trials, as well as immunomodulatory studies ancillary to HPV vaccine development. Work includes collaboration with investigators from academic institutions and international pharmaceutical companies, and development of programmatic support coordinating trials to test different vaccine models. Two team members are also working with DCEG on a prophylactic HPV vaccine clinical trial. A Team member currently serve as medical monitor for a project that relates to HPV 16 vaccine effect on the reduction of viral load in HPV 16-positive women with persistent viral infection but low grade disease (ASCUS/LSIL).

Team members also serve as resources for other breast and gynecologic cancer issues, through review of publication articles, grant and contract review, and as speakers at various programs. The BGCRG is a small team that carries a large punch towards pre-empting breast and gynecologic cancers, or at least towads discovering and identifying agents that will put us on the path of preventing these devastating women cancers. ■

The Contract as a Funding Mechanism continued from page 2

allows the funding of the early phase studies that are necessary for the development of specific chemopreventive agents but are not likely to be funded through peer review and may not be attractive to industry. Peer-reviewed funding for prevention phase I and phase II studies with biomarker endpoints is difficult to obtain, even though these studies supply critical information necessary for making informed decisions about subsequent phase III efficacy trials. Pharmaceutical companies are also frequently not interested in funding such trials because typically they do not lead quickly to profitable new agents. Second, the setting up and conduct of such investigative studies is frequently too complex for a single academic institution, requiring multiple sites to accrue the appropriate subject cohorts and thereby making the studies less appropriate for peer-reviewed funding. The contract mechanism was chosen, in part, because it could provide the funding that is required for the development of the necessary infrastructure at each of the six chosen institutions.

The six institutions that form the newly established DCP Prevention Consortia are The University of Arizona, The University of California at Irvine, The Mayo Clinic, The Universtiy of Texas M.D. Anderson Cancer Center, Northwestern University, and The University Wisconsin—Madison. These centers were selected as the result of a request for proposals (RFP) for infrastructure development. These became effective last October. Now that the infrastructure is in place at each institution, the funding of the phase I/II trials of selected agents will continue on a rolling schedule in the form of requests for Letters of Intent to perform chemoprevention studies. New agents will be announced three to four times per year. The new Prevention Consortia are beginning work on a variety of studies aimed at different target organs, using atorvastatin, green tea polyphenols, nitric oxide-releasing aspirin (NO-ASA), RAFTILOSE, Synergy1, rofecoxib, soy isoflavones, and sulindac.

The authors owe special thanks to Ann O'Mara and Linda Parreco for helpful discussions. ■

DOUGLAS MIDTHUNE

Christine D. Berg, M.D., has joined DCP as Chief of the Early Detection Research Group. In this position, she is Project Officer for the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (PLCO) and the National Lung Screening Trial (NLST), and has responsibility for the utilization of the PLCO Biorepository. For 3 years prior to accepting this position she served as Medical Director of the Suburban Hospital Cancer Program, Bethesda, Maryland. Prior to joining Suburban Hospital she was Chief of the Lung and Upper Aerodigestive Cancer Research Group at DCP, and for 15 years served in leadership positions, including Director, Breast Radiation Therapy, and Residency Training Director, at the Lombardi Cancer Center, Georgetown University Medical Center. Originally from Chicago, Dr. Berg earned her B.S. and M.D. in Medical Education, Northwestern University Medical School. She completed her internship and residency in Internal Medicine at Northwestern Memorial Hospital, Chicago, and served as Chief Resident of Internal Medicine. After a fellowship in Medical Oncology at NCI, she completed her residency in Radiation Oncology at Georgetown University Medical Center. Dr. Berg is board certified in Internal Medicine, Medical Oncology and Radiation Oncology.

Daniel Boring, R.Ph., Ph.D., recently joined the Chemopreventive Agent Development Research Group as a Program Director. Dan began his career as a pharmacist, graduating from the University of Houston, College of Pharmacy. He has been a registered pharmacist for 30 years and continues to practice pharmacy on weekends. Dan earned a doctorate in medicinal chemistry at the University of Mississippi ("Ole Miss") and subsequently did postdoctoral work at NIH in the Laboratory of Drug-Receptor Interactions, before becoming an assistant professor at the University of Missouri, College of Pharmacy. For the past 14 years, Dr. Boring was a primary chemistry reviewer at the Center for Drug Evaluation and Research (CDER) at FDA. He also was the Center Expert in Labeling and Nomenclature, the Chair of the CDER Labeling and Nomenclature Committee, and the Chair of the Chemistry Peer Review Committee. Dan has published widely in both scientific and regulatory journals, and is proud to note that his first scientific paper, over 25 years ago, was based on research in cyclic nitrosoureas to be used as oncolytics.

Mahin Khatami, Ph.D., has joined the Cancer Biomarkers Research Group as a Health Science Administrator. She earned her B.S. in chemistry and M.A. in Science Education in Iran, her M.S. in Biochemistry at SUNY/Buffalo, and her Ph.D. in Molecular Biology at the University of Pennsylvania. For several years, Mahin was a member of the Research Faculty of Medicine at the University of Pennsylvania. She also served as a Research Associate at Fox Chase Cancer Center and the University of Pennsylvania, as an Advisor for Research and Chairman of the Biochemistry Department at the Pasteur Institute of Iran, and as Professor of Pharmacology at Tehran University. During 1998 and 1999, she served as Health Science Administrator and Program Director in the Early Detection Research Group in DCP. Her research interests include cancer biology and immunology, cellular/molecular and immunological mechanisms of angiogenesis in inflammation, diabetes and cancer, and evaluation of chemopreventive agents and cancer biomarkers.

Antoinette Wills recently joined the Administrative Resource Center as an Administrative Technician. Antoinette comes to DCP from the National Institute of Dental and Craniofacial Research, where she had worked since 1997. Prior to joining NIDCR, she spent 10 years at the Department of Veterans Affairs Medical Center in Washington, D.C., where she began her federal government service as a stay-in-school student.

BEST WISHES TO:

Joyce Browne worked with the Early Detection Research Group for 12 of her 30+ years of federal service before retiring last January. She served as the Project Coordinator for the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial from its beginning. She now fills her time volunteering in the community and pursuing her interests in her Native American heritage.

Jill Hughes retired in July after 4 years as an Administrative Program Assistant in the Administrative Resource Center. She's returning "back home" to Alabama and intends to devote a good portion of her time spoiling an expanding brood of grandchildren.

Nancy Simpson retired in March as a Public Health Advisor in the Early Detection Research Group. Although she has entered the retirement phase of her life, we are certain she will continue her enthusiastic participation in all future endeavors, such as national and international public health projects. In addition, she has been traveling with her husband throughout Asia, and is enjoying spending time with her family and remodeling her home.

Heide Weaver recently retired as Program Specialist in the Office of Preventive Oncology. She joined DCP in 1999, and worked at NIH for 20 years. Originally from Germany, Heide's plans include traveling and volunteering in a museum.

Rose Mary Padberg, R.N., recently left DCP, after 13 years as Special Assistant in the Office of the Associate Director. Rose Mary credits her time working on major prevention trials with Dr. Leslie Ford with preparing her for the challenges of her new position as Chief of Cancer Education in the NCI's Office of Education and Special Initiatives.

Other employees leaving DCP include **Tracy Ellis, Stephen Carrington, Mukesh Verma, Charmaine Boswell, Myra Terrell,** and **Raheleh Amini**. We wish all our colleagues well in their new endeavors.

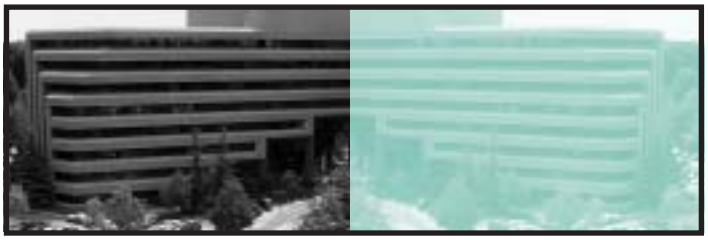
OF NOTE:

David Levin, M.D., longtime member of the Biometry Research Group, recently retired as Commissioned Officer in the US Public Health Service. Dave continues to work in BRG, now as a civil servant.

Kay Simmons, National Program Leader for Grain Crops Research at the Agricultural Research Service, USDA, spent March and April of this year at DCP with the Nutritional Science Research Group, on detail as part of the Senior Executive Service candidate development program. Kay planned to use her time here to develop alliances or partnerships to improve the health benefits of grains.

Annual Advances in Cancer Prevention Lecture

The fifth Annual Advances in Cancer Prevention Lecture, sponsored by the Cancer Prevention Fellowship Program, was held in the Lister Hill auditorium on the main NIH campus in Bethesda, Maryland, on July 29. Dr. Andrew von Eschenbach, Director of the National Cancer Institute, introduced the featured speaker, Dr. Waun Ki Hong of the University of Texas M.D. Anderson Cancer Center in Houston, Texas. Dr. Hong, one of the founders of cancer chemoprevention and a world-renowned expert in the treatment of head, neck, and lung cancer, presented the keynote lecture, entitled "Convergence of Molecular Targets for Cancer Prevention and Therapy." The lecture was followed by a reception in Lister Hill. ■



DCP home base: Executive Plaza

At the Forefront of Training

SUSAN WINER

Time has passed quickly, and our first-year fellows arrived at the NCI this summer to begin their research after completing Master of Public Health programs. Recent graduates from the Johns Hopkins Bloomberg School of Public Health are Drs. Charles Baffi, Camille Hammond, Karla Lawson, Haruhito Murata, and Krista Zanetti. Drs. Keith Bellizzi and JaMuir Johnson graduated from George Washington University. Returning from the Harvard School of Public Health are Drs. Martha Hunt and Melissa Miller. Dr. Elizabeth Bluhm completed her M.P.H. at the University of North Carolina at Chapel Hill and Dr. Paul Han completed his at the University of Pittsburgh. The Cancer Prevention Fellowship Program (CPFP) also welcomed five fellows who came directly to the NCI to begin their research. These fellows are Drs. Cara Frankenfeld, David Haggstrom, Simon Lee, Annette Molinaro, and Leah Sansbury.

This year's CPFP orientation week for incoming fellows featured a variety of important topics, including time management, banking and tax information, NIH's email system, and computer resources. Presentations were made by the NCI Ethics Office and the Division of Cancer Prevention's Administrative Office. Another important feature of orientation week is the opportunity for presentations by potential research preceptors. This year the following NCI divisions were represented: Division of Cancer Prevention, Division of Cancer Control and Population Sciences, Division of Cancer Epidemiology and Genetics, and Center for Cancer Research. In addition, the incoming fellows attended orientation sessions with the CPFP staff, as well as with senior fellows.

The five-week NCI Summer Curriculum in Cancer Prevention began on July 6th, following orientation. This world-renowned Summer Curriculum in Cancer Prevention comprises two courses: Principles and

continued on page 11

Dr. Peter Greenwald, Director of the Divison of Cancer Prevention, addresses the Cancer Prevention Fellows during the Cancer Prevention Fellowship Program Orientation Week, June 21 - 25, 2004.

NCI Summer Curriculum in Cancer Prevention - Group Photo.

AWARDS

Congratulations to the following fellows, who received the National Cancer Institute's Cancer Prevention Research Training Merit Award for 2004: Drs. Somdat Mahabir, Nomelí Núñez, and Shanita Williams-Brown.

In addition, fellows received the following awards:

Dr. Julie Goodman, second-year fellow: Honorable Mention for her poster presentation, entitled "*ALOX* and *COX* Polymorphisms andColon Cancer Risk: Associaiton with *ALOX-5* G-1753A & G1700A," at the NCI Center for Cancer Research Annual Fellows and Young Investigators Retreat, held in Williamsburg, VA, March 2004.

Dr. Tamaro Hudson, second-year fellow: selected to attend the American Association for Cancer Research's Edward A. Smuckler Memorial Pathobiology of Cancer Workshop held in July 2004 in Snowmass Village, CO.

Dr. Martha Hunt, first-year fellow: the Garreth Green Public Health Practice Award for her practicum project at the Harvard School of Public Health, Boston, MA.

Dr. Larissa Korde, second-year fellow: the Excellence in Special Project Award in Epidemiology and Biostatistics from the George Washington University, Washington, DC.

Dr. Jill Reedy, first-year fellow: Honorable Mention Poster Award at the American Society for Preventive Oncology Annual Conference held in Bethesda, MD, in March 2004. Her title was "Influence of Health Behavior Clusters on Dietary Change among Colorectal Cancer Survivors." Dr. Reedy also received the A. Hughes Bryan Outstanding Doctoral Award, Department of Nutrition, University of North Carolina at Chapel Hill, Chapel Hill, NC. In addition, Dr. Reedy was inducted into the Delta Omega Honorary Society in Public Health, Theta Chapter, School of Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC.

Best wishes for continued success in your careers in cancer prevention and control!

ON THE PERSONAL SIDE

Congratulations to JaMuir Johnson on her marriage to Jason Robinson and to Whitney Randolph on her marriage to Michael Steele.

At the Forefront of Training continued from page 10

Drs. Missy Miller, Karla Lawson, and David Haggstrom participate in the Molecular Prevention Laboratory for CPFP Fellows.

Practice of Cancer Prevention and Control, and Molecular Prevention. Approximately 100 clinicians and scientists from around the world were in attendance. Countries represented in this year's Summer Curriculum included Jordan, Saudi Arabia, Turkey, China, Japan, Nepal, Russia, Nairobi, Brazil, Costa Rica, Lithuania, Northern Ireland, Republic of Ireland, and the United Kingdom. In addition, fifteen Cancer Prevention Fellows and other NCI clinicians and scientists attended the courses.

This summer and fall nine new Cancer Prevention Fellows will begin their M.P.H. training at the following institutions: the Johns Hopkins Bloomberg School of Public Health – Drs. Ellen Beckjord, Jiping Chen, Damali Martin, Susan Olivo Marston, and John Tyburski; University of California at Berkeley –Dr. Aaron Schetter; George Washington University – Dr. Jessica Faupel-Badger; Columbia University – Dr. Jonine Figueroa; and Harvard University – Dr. Neal Freedman.

This year's recruitment for the CPFP has been busy, with attendance at the American Association for Cancer Research meeting, held in March in Orlando, FL, and the American Society of Clinical Oncology meeting, held in June in New Orleans. The annual Cancer Health Disparities meeting was held in Washington, DC, in July. Recruitment materials for the CPFP are displayed in the NCI booth at other major cancer-related meetings, including Oncology Nursing, Society for Epidemiologic Research, and American Urology Association. ■

Beyond the Fellowship Program

Congratulations and best wishes to the following fellows who have recently completed the CPFP:

Dr. David Buchanan has returned to his position as Professor, Department of Community Health Education, at the University of Massachusetts in Amherst, MA.

Dr. Marla Clayman has accepted a position as Assistant Professor at Northwestern University's Feinberg School of Medicine in Chicago, IL.

Dr. Amanda Green has accepted a position as Senior Researcher at NOVA Research in Bethesda, MD.

Dr. LaKreis Kidd has accepted a position as Assistant Professor of Pharmacology and Toxicology in the School of Medicine and Assistant Professor in the James Graham Brown Cancer Center at the University of Louisville, in Louisville, KY. She will also be appointed to the James Graham Brown Foundation "Our Highest Potential" Chair in Cancer Research.

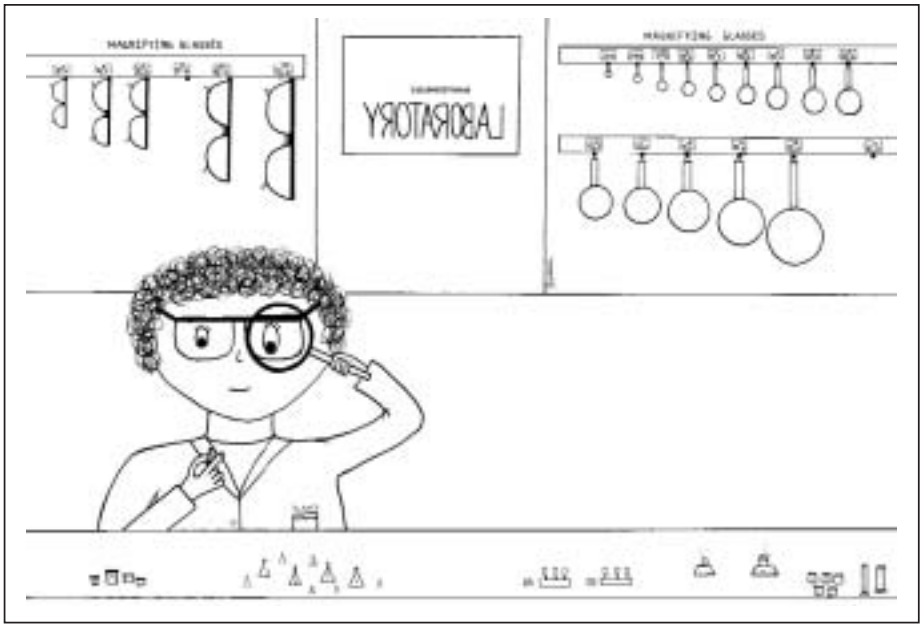
Dr. Leah Mechanic will be joining the Center for Cancer Research in the National Cancer Institute, Bethesda, MD.

Dr. Shanita Williams-Brown has accepted a position as Research Scholar at the National Center for Primary Care at the Morehouse School of Medicine in Atlanta, GA. In addition, she will have a faculty appointment as Assistant Professor in the Department of Community Health and Preventive Medicine.

Best wishes to all the fellows for continued success in the field of cancer prevention and control! ■

CARTOON

GRAÇA DORES



Nanotechnology Laboratory

DCP Awardees

GLORIA RASBAND AND SUSAN N. PERKINS

The following members of DCP were recognized by Dr. Peter Greenwald, DCP Director, at the 2004 Awards Ceremony for their length of service to the federal government:

10 YEARS OF SERVICE AWARDS

Terri Cornelison, James Crowell, Barbara Dunn, Richard Fagerstrom, Linda Gray, Ernest Hawk, Angela Green Jenkins, Victor Kipnis, Young Kim, Elizabeth McMillan, Lori Minasian, and Delta Joy Osborne

20 YEARS OF SERVICE AWARDS

Iqbal Ali, Christine Donati, J. Dianne Gary, Gloria Rasband, Vernon Steele, and Douglas Weed

30 YEARS OF SERVICE AWARDS

Joyce Browne, Phil Prorok

Congratulations to Dr. Peter Greenwald upon his 40th year of membership in the American Public Health Association. The Epidemiology Section will recognize Dr. Greenwald for his service and commitment to public health during the 132nd Annual APHA Meeting in Washington, DC, November 6-10, 2004.

RECENT, ONGOING, AND UPCOMING DCP EVENTS

DATE	TOPIC	DESCRIPTION	WEBSITE
SEPTEMBER – JUNE 2004-2005	2004-2005 Colloquia Series	The Office of Preventive Oncology presents a Colloquia Series on Wednesdays from 11:00 a.m. to noon.	http://www3.cancer.gov/prevention/pob/fellowship/colloquia.html
JULY 6-30, 2004	Principles and Practice of Cancer Prevention and Control Course	This annual four-week summer course focuses on the concepts, methods, issues, and applications related to the principles and practice of cancer prevention and control. Participants have the opportunity to gain a broad-based perspective of these subjects, including resources, data, methods, and theories.	http://www3.cancer.gov/prevention/pob/courses/principles.html
JULY 28-29, 2004	Workshop: Research Strategies, Study Designs and Statistical Approaches to Biomarkers Validation for Cancer Diagnosis and Detection	Held in cooperation with the Food and Drug Administration (FDA), the Cancer Biomarkers Research Group sponsored this workshop to review various aspects of biomarker validation, especially as related to statistical considerations, and to discuss FDA guidelines.	http://www3.cancer.gov/prevention/cbrg/events.html
JULY 29, 2004 3:00 P.M. LISTER HILL AUDITORIUM	Annual Advances in Cancer Prevention Lecture	Waun Ki Hong, M.D., U. Texas M.D. Anderson Cancer Center. "Convergence of Molecular Targets for Cancer Prevention and Therapy."	http://cancer.gov/prevention/pob
AUGUST 2 - 6, 2004	Molecular Prevention Course	This annual course provides a strong background in the molecular biology and genetics of cancer as well as an overview of the basic laboratory approaches applied to cutting-edge research in the fields of molecular epidemiology, bionutrition, chemoprevention, biomarkers, and translational research.	http://www3.cancer.gov/prevention/pob/courses/molprev.html
SEPTEMBER 20, 2004 4:00 P.M. LISTER HILL AUDITORIUM	Stars in Nutrition and Cancer Seminar Series	Dr. Robert Evans, "Nuclear Receptors and the Complex Journey to Obesity."	http://www3.cancer.gov/prevention/nrcjo/index.html
JANUARY 16-21, 2005	Gordon Research Conference on New Frontiers in Cancer Detection and Diagnosis	TBA	http://www.grc.uri.edu/05sched.htm
MARCH 2005	Site Coordinators' Opportunity for Research Excellence (SCORE 2005)	The objectives for this annual workshop are to provide ongoing education and training for site coordinators and staff working on DCP chemoprevention protocols.	www3.cancer.gov/prevention/score/